REMARKS

Claims 1-22 were pending prior to this response. By the present communication, claims 1, 2, 10, 11 and 17-22 have been amended and new claims 23-28 have been added to define Applicants' invention with greater particularity; no claims have been deleted. The amendments add no new matter, being fully supported by the Specification and original claims. Support for new claims 23-28 is found in paragraph 42 of the Specification at page 14. Accordingly, claims 1-28 are presently pending.

The Rejection Under 35 U.S.C. § 102(e)

Applicants respectfully traverse the rejection of claims 1-4, 6-14 and 16-21 under 35 U.S.C. § 102(e) over Leone et al. (U.S. Patent No. 5,505,700; hereinafter "Leone"). Applicants note that claim 5, pertaining to a catheter having a guidewire as a second electrode, and claim 15, pertaining to a catheter having a silver plate as a second electrode, are not included among the rejected claims. Yet, the Examiner has made specific comments regarding Leone's disclosure of a guidewire in the catheter being a second electrode (Office Action, page 2). Accordingly, Applicants' following remarks are based on the assumption that the Examiner intended to include claim 5 in the present rejection, and exclude from the rejection claims 6, 15 and 22, the three dependent claims that recite "wherein the second electrode is a silver plate ....". Should this assumption be in error, Applicants request the Examiner to so advise Applicants' representative by telephone.

Applicants respectfully submit that the invention apparatus for introducing a composition into at least one cell in a vessel in a subject, as defined by claims 1, 10, and 17, and claims dependent therefrom, distinguishes over the disclosure of Leone. In part, present claims 1, 10, and 17 recite that the invention catheter has a first and second electrode "wherein said first and second electrodes are suitable to receive an electric pulse having an electroporating voltage in the range of about 10 Volts to 200 Volts and having a pulse length of about 100 microseconds to 100 milliseconds, and wherein said second electrode is proximally positioned with respect to the first electrode and the subject such that when the electric pulse is applied to the first and second electrodes an electric field is generated in the subject of between 0.5 and 5.0 kV/cm, which is sufficient to cause electroporation of at least one cell in the vessel before, during or after introduction of the composition into the subject through the at least one infusion opening." Leone is absolutely silent regarding a catheter, or the design requirements of a catheter, that is suitable for receiving an electric pulse and administering an electric field according to all elements of present claims.

Instead, Leone discloses a drug infusion catheter designed for use in iontophoresis or iontohydrokinesis of ionically charged substances. Intophoresis/iontohydrokinesis is effected through application of a low voltage, low current over a relatively long period of time, for example 10 minutes, such that an ionically charged medicament fluid moves away from a like-charged internal electrode (Leone, col.4, ln 54-56). This process is different from electroporation, and different from the presently claimed invention, which is effected by application of short electric pulses (e.g., pulse length of 100 microseconds to 100 milliseconds) of relatively high

voltage (e.g., voltage in the range of about 10 Volts to 200 Volts) to at least two electrodes, such that an electric field of sufficient strength to cause electroporation results (e.g., an electric field of about 0.5 and 5.0 kV/cm).

Similarly, the placement of electrodes used in an electroporation apparatus, including the presently claimed apparatus, differs from the placement of electrodes used for iontophoresis. For iontophoresis, it is not necessary that electrodes, such as Leone's internal and integral electrodes, be in close proximity to each other. In contrast, the electrodes of the invention apparatus, which is used for electroporation, are proximally placed so a field strength sufficient for electroporation can be generated between and around the electrodes. Leone is silent regarding the placement of the first and second electrodes so as to suitable for use of the apparatus for electroporation. Indeed, all of Leone's illustrations fail to disclose a second electrode that "is proximally positioned with respect to the first electrode and the subject such that when the electric pulse is applied to the first and second electrodes an electric field is generated in the subject of between 0.5 and 5.0 kV/cm," as is recited in the present claims.

Because Leone fails to disclose each and every element of claims 1, 10, and 17, Leone also fails to disclose each and every element of claims dependent therefrom. Accordingly, the comments above are made in response to the rejections of the independent claims, as well as the Examiner's comments with respect to certain dependent claims.

Notwithstanding the foregoing, Applicants specifically disagree with the Examiner's assertion that Leone discloses a catheter wherein the guidewire is a second electrode at Col 4, line 63 (Office Action, page 2). The passage referred by the Examiner reads as follows:

> While the electrodes 35, 36 are illustrated as either a coiled wire or a wire band, either electrode component could take on either configuration and can include additional or alternate configurations such as longitudinally directed veins, conductive meshes, conductive coatings applied by deposition or the like, ...

This passage does not recite use of a guidewire as an electrode. Leone's sole comment regarding a guidewire does not describe the guidewire as an electrode. In fact, Leone does not describe a guidewire as being electrically conducting at all:

> A central lumen 28 can be provided as illustrated in order to accommodate a guidewire (not shown), for example, or for some other purpose that requires a lumen passageway through the catheter.

(Leone, Col 4, lines 38-42). Thus, Applicants submit that Leone does not disclose use of a guidewire as a "second electrode" as asserted by the Examiner.

Applicants submit that because Leone fails to disclose a catheter or apparatus having each and every element of the rejected claims, as would be required to establish anticipation under 35 U.S.C. § 102(e), the rejection is moot. Accordingly, Applicants request reconsideration and withdrawal of the rejection.

The Rejection under 35 U.S.C. § 103

Applicants respectfully traverse the rejection of claims 6, 15, and 22 under 35 U.S.C. § 103 over the combined disclosures of Leone as above and Shapland et al. (U.S. Patent No. 5,634,899; hereinafter "Shapland"). Claims 6, 15 and 22, which depend from claims 1, 10, and 17, respectively, recite that the second electrode of the apparatus or catheter of the independent claim is a silver plate configured to be placed in contact with the subject. The Examiner acknowledges that Leone does not disclose this subject matter, although Leone broadly discloses that electrodes may take on alternate configurations. Shapland is cited as teaching that the material of a remote electrode used with a catheter for electroporation may be silver. It is the Examiner's position that it would have been obvious to use a silver remote electrode taught by Shapland as the second electrode in the Leone inventions.

The invention apparatus or catheter for introducing a composition into at least one cell in a vessel in a subject, as defined by claims 1, 10, and 17, and further by claims 5, 15 and 22 that are dependent therefrom, distinguishes over the disclosure of Leone for at least the reasons stated above in response to rejection under 35 U.S.C. § 102(e). The Shapland disclosure does not address all omissions in the Leone disclosure and therefore does not cure the deficiencies in the Leone disclosure.

In particular, with respect to claims 6, 15 and 22, the Shapland electrode made of a coil of silver wire, pointed to by the Examiner, is different than the silver plate recited in claims 6, 15

and 22. Not only is that citation directed to a coil electrode provided around the body of the catheter (not on the body of a subject), but Shapland does not teach or suggest a "silver plate" electrode as recited in claims 6, 15 and 22. Any suggestion by Shapland that silver can be used as an electrode in a catheter is not sufficient to suggest modification of the Leone catheter to comprise a silver plate electrode for application to a subject's body.

Moreover, based on the Leone disclosure, one of ordinary skill in this art would not be motivated to look to Shapland to find the silver plate electrode recited in the rejected claims. Leone casts his invention as a solution to the problem that can occur when an electrode that contacts the subject is used for iontophoresis, i.e., electrical current passes through the body. The Leone iontophoresis device, which comprises an internal electrode and an electrode integral with the catheter, is said to solve this problem. Regarding placement of electrodes, Leone states:

> In accordance with the present invention, the undesirable aspects of having to pass the electric current through body tissue because of the potential set up between an internal electrode and an external return electrode are eliminated. Instead, an internal electrode is combined with another electrode which is positioned on the catheter itself, which is considered to be integral with respect to the catheter.

(column 2, lines 20-26). Thus, because Leone teaches that it is undesireable to have an external electrode, one of skill would not be motivated to combine the Shapland teaching of an external electrode with the Leone teaching that directs a user away from a body surface electrode, to reach the apparatus of present claims 6, 15, and 22.

In view of the differences between the invention apparatus, as defined by claims 1, 7 and 14, and claims 6, 15, and 22, and the disclosure of Shapland, as well as the lack of motivation to combine the references, Applicants submit that *prima facie* obviousness under 35 U.S.C. § 103 of the invention apparatus is not established over the combined disclosures of Leone and Shapland and reconsideration and withdrawal of the rejection are respectfully requested.

In view of the above amendments and remarks, consideration and favorable action on claims 1-28 are respectfully requested. If the Examiner would like to discuss any of the issues raised in the Office Action, the Examiner is encouraged to call the undersigned so that a prompt disposition of this application can be achieved.

Respectfully submitted,

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Enclosure: Exhibit A

PATENT
ATTORNEY DOCKET NO.: GENE1180-2

Applicants: Dev, et al.
Application No.: 10/020,531
Filed: December 14, 2001
Exhibit A: Page 1

EXHIBIT A

Version with Markings to Show Changes Made

In the claims

1. (Twice Amended) An apparatus for introducing a composition into at least one cell in a vessel in a subject comprising:

a catheter having at least one inflatable balloon portion[, wherein upon inflation, the balloon portion occludes the vessel];

at least one infusion opening for introducing the composition into the subject proximal to the at least one inflatable balloon portion;

a first electrode positioned adjacent to at least one infusion opening; and

a second electrode, wherein said first and second electrodes are suitable to receive an electric pulse having an electroporating voltage in the range of about 10 Volts to 200 Volts and having a pulse length of about 100 microseconds to 100 milliseconds, and wherein said second electrode is proximally positioned with respect to the first electrode and the subject such that when the electric pulse is applied to the first and second electrodes an electric field is generated in the subject of between 0.5 and 5.0 kV/cm, which is sufficient to cause electroporation of at least one cell [is generated, thereby allowing the composition to enter at least one cell] in the vessel before, during or after introduction of the composition into the subject through the at least one infusion opening.

2. (Amended) The apparatus of claim 1, further comprising an electrical source connected to the first and second electrodes for applying the electric pulse to [a voltage between] the electrodes [in an amount sufficient to cause electroporation of at least one cell].

10. (Amended) A catheter comprising:

a first inflatable balloon portion near the distal end of the catheter;

a second inflatable balloon portion proximal to the first inflatable balloon, wherein inflation of the first and second balloon portions occludes a vessel between the first and second balloon portions;

at least one infusion opening for introducing a composition into a subject located between the first and second balloon portions;

a first electrode positioned adjacent to or integral with at least one infusion opening; and

a second electrode, wherein said first and second electrodes are suitable to receive an electric pulse having an electroporating voltage in the range of about 10 Volts to 200 Volts and having a pulse length of about 100 microseconds to 100 milliseconds, and wherein said second electrode is proximally positioned with respect to the first electrode and the subject such that when the electric pulse is applied to the first and second electrodes an electric field is generated in the subject of between 0.5 and 5.0 kV/cm, which is sufficient to cause electroporation of at least one cell before, during or after introduction of the composition through the at least one infusion opening.

11. (Amended) The catheter of claim 10, further comprising an electrical source connected to the first and second electrodes for applying [a voltage between] the electric pulse to the electrodes [in an amount sufficient to cause electroporation of at least one cell].

17. (Amended) An apparatus for introducing a composition into at least one cell in a vessel in a subject comprising:

a catheter having at least one inflatable balloon portion at a position other than the distal end of the catheter;

at least one infusion opening for introducing the composition into the subject;

a first electrode positioned adjacent to at least one infusion opening; and

a second electrode, wherein said first and second electrodes are suitable to receive an electric pulse having an electroporating voltage in the range of about 10 Volts to 200 Volts and having a pulse length of about 100 microseconds to 100 milliseconds, and wherein said second electrode is proximally positioned with respect to the first electrode and the subject such that when the electric pulse is applied to the first and second electrodes an electric field is generated in the subject of between 0.5 and 5.0 kV/cm, which is sufficient to cause electroporation of at least one cell before, during or after introduction of the composition through at least one infusion passage [can be administered].

18. (Amended) The [catheter] apparatus of claim 17, further comprising an electrical source connected to the first and second electrodes for applying [a voltage between] the electric pulse to the electrodes [in an amount sufficient to cause electroporation of at least one cell].

19. (Amended) The [catheter] apparatus of claim 17, wherein the vessel is a blood vessel.

20. (Amended) The [catheter] apparatus of claim 17, wherein the first electrode is formed at least in part by a biologically inert material.

21. (Amended) The [catheter] apparatus of claim 17, wherein the second electrode is a guidewire in the catheter.

22. (Amended) The [catheter] apparatus of claim 17, wherein the second electrode is a silver plate configured to be placed in contact with the subject.

Please add the following new claims:

--23. (New) The apparatus of claim 1, wherein the first electrode and the second electrode is separately selected to be a single electrode or multiple electrodes.

24. (New) The apparatus of claim 23, wherein the multiple electrodes are interdigitated electrodes or concentric ring electrodes.

25. (New) The catheter of claim 10, wherein the first electrode and the second electrode is separately selected to be a single electrode or multiple electrodes.

26. (New) The apparatus of claim 25, wherein the multiple electrodes are interdigitated electrodes or concentric ring electrodes.

27. (New) The apparatus of claim 17, wherein the first electrode and the second electrode is separately selected to be a single electrode or multiple electrodes.

28. (New) The apparatus of claim 27, wherein the multiple electrodes are interdigitated electrodes or concentric ring electrodes. --